Median mass aerodynamic diameter (MMAD) and fine particle fraction (FPF): influence on lung deposition?

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Rationale
The influence of particle size on lung deposition (LD) and efficacy with inhaled drugs is increasingly discussed, yet the role of the FPF is often overlooked. FPF is the fraction of the total drug dose <5.0μm; MMAD is the average size of particles constituting the dose which reach the impactor, excluding those that deposit in the ‘throat’. This study investigated the influence of FPF and MMAD on LD using Functional Respiratory Imaging (FRI).

Methods
3D airway models of 6 asthma patients (mean FEV₁ 83%) were included. Total lung (TLD), central (C) and peripheral (P) airway deposition of a monodisperse model aerosol with MMAD of 1.5-4.5μm (geometric SD=1.20) and FPF of 10-40% delivered by a pMDI were assessed with FRI (inhalation volume: 3L; time: 3s; actuation start of inhalation).

Results
TLD as % of nominal dose for each permutation of model aerosol are shown in the table.

<table>
<thead>
<tr>
<th>MMAD (μm)</th>
<th>40%</th>
<th>30%</th>
<th>20%</th>
<th>10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>34.05</td>
<td>25.54</td>
<td>17.03</td>
<td>8.51</td>
</tr>
<tr>
<td>3.0</td>
<td>32.47</td>
<td>24.35</td>
<td>16.23</td>
<td>8.12</td>
</tr>
<tr>
<td>4.5</td>
<td>33.58</td>
<td>25.18</td>
<td>16.78</td>
<td>8.39</td>
</tr>
</tbody>
</table>

The C/P ratio for MMAD of 1.5, 3.0 and 4.5μm were 0.42, 0.69, and 1.39.
Conclusions

FPF had a large impact on TLD in vitro whereas MMAD had little effect, although MMAD had some influence on C and P deposition: both 1.5 and 3.0μm MMAD profiles deposited mainly in P (C/P<1.0); 4.5μm aerosol deposited more in C airways (C/P>1.0). Many inhaled respiratory drugs need to reach both P and C airways but the optimal delivery between these for different classes of drugs is less understood. These data highlight the importance of FPF on TLD; beneficial drug effects often attributed to small particle size may really be a consequence of high FPF.

This study was funded by MundiPharma International